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November 22, 2000

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane R.1061
Rockville, MD. 20852

Re: Docket No. 00N-1367: Comment on Proposed Postmarket Surveillance Rule

Dear Sir or Madam:

Cook Group, Inc. submits the following comments on the proposal referenced above. Our major concern is FDA's assertion that 10% of postmarket surveillance may constitute clinical studies. Congress was clear that FDA should not interpret its postmarket surveillance authority to require such studies. In addition, we are concerned that the proposed rule's reporting requirements are not authorized by the Act's postmarket surveillance provision and that they will be unduly burdensome in contravention of section 519(a)(4) of the Act. Third, while we agree with FDA's goal of making the regulation understandable, in one case FDA incorporates a guidance document as substance, an apparent violation of notice and comment requirements. Fourth, the dispute resolution mechanism to resolve differences relating to postmarket surveillance obligations of greater than three years must be impartial and not weighted towards FDA. We discuss these and other issues below.

Meeting with FDA

In the preamble to the regulation, FDA acknowledges that 30 days may be insufficient to design and submit a surveillance plan. The agency notes that it may therefore request a meeting with the affected manufacturer prior to issuing a surveillance order, especially when the order is the first for a particular device. 65 Fed. Reg. 52376, 52379 (August 29, 2000). We believe that manufacturers that may be subject to a postmarket surveillance order should have an opportunity to meet with FDA as a matter of course and that such an opportunity should be incorporated into the regulation itself. As FDA notes, the purpose of the meeting would be to discuss the surveillance question and the possible approaches for the surveillance. All parties could benefit from such a meeting. It is our view that such meetings should be broadly available.

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Plain Language Format

While we applaud the agency's efforts to make the regulation understandable, some of the language used is more appropriate for a guidance document than for a legally binding regulation. For example, in § 822.23, FDA states that "[w]e consider the content of your submission confidential until we have approved your postmarket surveillance plan." Given our understanding of how FDA and the rules governing confidentiality work, we this should mean that FDA will not disclose the content of the submission until it has approved the plan. We believe the agency should make clear the binding nature of its commitment to nondisclosure of confidential materials. We suggest that FDA revise this section accordingly using language similar to that used in § 807.95, which specifies that the agency will not disclose confidential information in submissions publicly. Importantly, the agency should closely review the regulation to ensure it clearly communicates those things which are mandatory and those which are not.

Incorporation of Guidance as Substance of Regulation

Proposed 21 C.F.R. § 822.12 appears to incorporate FDA guidance into the regulation. We believe that this is inappropriate and without legal support. Although FDA uses Good Guidance Practices (GGPs), GGPs fall short of the procedures required by the Administrative Procedures Act (APA), 5 U.S.C. § 553. Section 553 of the APA requires that agencies use notice and comment procedures to promulgate regulations and changes to regulations. In contrast, even under GGPs, guidance documents can be issued and revised without addressing comments, and in some instances without even giving interested persons an opportunity for comment. The regulation's reference to guidance documents inaccurately suggests the guidance documents contain information necessary for compliance with the regulation. We believe referencing guidance in the regulation is confusing at best and illegal at worst. Therefore, we request that the reliance on guidance be discontinued in any final postmarket surveillance regulation.

Reference to Section 519(a) and Reporting Obligations in § 822.38

FDA relies upon § 519(a) of the Act for the reporting requirements included in the proposed postmarket surveillance regulation. 65 Fed. Reg. at 52378. Unlike § 522, which is self-implementing, § 519(a) must be implemented by regulation, subject to numerous conditions precedent.

Specifically, we question the appropriateness of grafting postmarket surveillance requirements onto a statutory authority that relates explicitly to a particular type of reporting authority already implemented in the MDR regulation. More importantly, we question whether the agency has observed in this proposal the clear limits on FDA's rulemaking authority under § 519. In particular, section 519(a)(4) prevents FDA from imposing record-keeping or reporting requirements that are "unduly burdensome." We ask that the agency expressly address whether the regulation is unduly burdensome and, if so, address the excessive burden. Without satisfying this statutory requirement, any final regulation's reporting requirement, which relies upon section 519 authority, will be illegal.

Clinical Studies

We believe any requirement FDA's postmarket surveillance authority does not support a requirement for clinical studies. In the preamble of the proposal, FDA estimates that 10% of postmarket surveillance will require "primary data collection" meaning clinical trials, 50% may utilize secondary data sources, and 40% may collect adequate data from published reports.[1] Section 522 does not authorize FDA to impose postmarket clinical trials on any subset of manufacturers subject to postmarket surveillance orders. Congress intended that, in light of FDA's significant authority to require clinical data in marketing applications, the agency should apply § 522 as a complementary authority, permitting the monitoring of marketed devices under conditions of actual use.

Section 522 as originally enacted in 1990 referred to a "protocol for the required surveillance." This language was deliberately changed in 1997 to "a plan for the required surveillance" to make clear that postmarket surveillance was not intended to require clinical trial protocols. Moreover, the reference to the collection of data and information "to provide safety and effectiveness information for the device" was deleted to clarify the relationship between premarket studies and postmarket surveillance. While FDA uses the former to establish the safety and effectiveness of a device prior to marketing, the agency uses the latter to collect information on adverse events that occur during actual use of the device after commercial distribution. The legislative history of the 1990 and 1997 laws demonstrates that postmarket surveillance was not meant to require clinical trials. The legislative history in 1990 repeatedly refers to postmarket surveillance as the early monitoring of actual clinical experience with the device in contrast to controlled clinical trials done under FDA's premarket review authority. Nevertheless, confusion regarding FDA's authority under the provision led Congress to make explicit in 1997 that it did not intend FDA's postmarket surveillance authority to allow the agency to impose requirements for clinical studies in the postmarket context.

1990

Specifically, postmarket surveillance is described in the 1990 Conference Report as one of the "provisions that require manufacturers to conduct monitoring of clinical experience with certain devices soon after they are first marketed." Conf. Rep. page 26 (emphasis added). The House Committee Report also speaks of postmarket surveillance as requiring "FDA to monitor the performance of every permanently implanted device . . . and every other device intended for use in supporting or sustaining human life . . ." Pages 31-32. The Senate showed the same understanding of postmarket surveillance as a monitoring requirement rather than as an authority for imposing postmarket clinical trials when it stated that "the Committee intends this section to allow for clinical monitoring of the earliest experiences with a device once it is distributed in the

[1] FDA acknowledges that "primary data collection utilizing clinical trials will generally be impractical because of difficulties obtaining patient and clinician participation. In addition, this type of data collection would have significant resource requirements." 65 Fed. Reg. 52382. Nevertheless, FDA continues and says that "Primary data could, however, be used to survey smaller populations, or populations that could experience relatively high rates of adverse events." Id. It also states that Parts 50 and 56 apply to studies and "this may include PS studies." Id. at 52379.

general population under actual conditions of use." page 29-30.[2] Senator Kennedy described it the same way in the Senate floor debate in noting the bill required "manufacturers of devices that may pose substantial risks to contract with qualified academic medical centers to monitor clinical experience." (excerpt from S12489, cols. 1 and 2, and S15210, col. 3). Senator Dodd used the "monitoring" language as well. Page S12494, col. 1.

Senator Coats distinguished between postmarket surveillance and clinical trials by stating:

> Equally important are the provisions that give the Secretary of Health and Human Services additional authority to monitor a product after it has been approved to ensure it performs correctly. No matter how carefully a device is reviewed in the approval process there are limits on what can be learned. Devices used in the approval process are custom made, the physicians using them in clinical trials are chosen for their expertise, and the patients used in clinical studies are selected to increase the chances of positive results. There is nothing wrong with this. In fact, the clinical trial procedure is in the best interest of all parties.
>
> However, there is a big difference between a custom-made device used in the approval process and a mass-produced device that is sold nationwide. . . Postmarket surveillance will be conducted for an appropriate period of time on similar devices so that deviations from expected performance can be recognized as soon as possible.
>
> S15211 (cols. 2 and 3).

The purpose of postmarket surveillance, then, was to permit FDA to gain information on devices in situations of actual use, as opposed to in the controlled environment of a clinical trial.

On the other hand, the legislative history mentions data and proper study design. House Committee Report, pages 31-32, and the Senate Committee Report states that "the Committee is aware of post-approval studies that are currently conducted for certain Class III products, as well as manufacturer-initiated efforts to determine product performance. The Committee anticipates that the Secretary will promulgate regulations that may allow, under appropriate circumstances, adaptations of such existing surveillance techniques in order to conform with the requirements of this section." pages 29-30 of Senate Committee report 1990. The legislative history also mentions data that would be collected and the protocols used to collect such data.

1997

Accordingly, in 1997, the statute was changed to replace the word "protocol" with the word "plan," to remove the connotation that a clinical study was contemplated. The legislative

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[2] See also, page 42 of the Senate Committee Report which describes postmarket surveillance as "monitoring of clinical experience."

history this time was quite explicit. As was stated in the Senate Committee Report (S. Rep. No. 105-43 (1997) (accompanying S830):

> Further, the committee is concerned that FDA not interpret the postmarket surveillance authority as power to require longitudinal studies for FDA approved products.

The proper time to require clinical studies is prior to clearance or approval, during the premarket process. FDA's statement that only 10% of its postmarket surveillance would require the primary collection of clinical data, i.e., clinical studies, is inconsistent with legislative history of FDAMA making clear that Congress did not intend § 522 as a means for the agency to require clinical studies on marketed devices. We therefore request that the agency clarify that its postmarket surveillance orders will require monitoring, literature reviews, and other forms of surveillance apart from clinical studies.

Maximum Period of Surveillance and Dispute Mechanism

The statute and the proposed regulation bind FDA to three years as the maximum period of surveillance the agency can unilaterally require. The agency can impose surveillance for an additional period only with the concurrence of the manufacturer, or by prevailing in the dispute resolution mechanism provided by § 562. Section 562, requires a regulation for its implementation, which FDA promulgated as an amendment to § 10.75.

FDA has released a guidance document on dispute resolution, which sets forth FDA's thinking on use of a Medical Devices Dispute Resolution Panel. The panel is to be composed of eight members – five standing members and three temporary voting members. Of the five standing members, one is to be a nonvoting consumer representative, and one is to be a nonvoting industry representative. The other three standing members will have general scientific expertise applicable to a broad range of scientific issues; biostatisticians and epidemiologists are examples of experts that could be appropriate. The three temporary voting members are to be chosen based on their experience, expertise or analytical skills relevant to the review of a particular disputed issue and will be drawn from current members of the Medical Devices Advisory Committee ("MDAC"), current special Government employees serving as consultants to the MDAC, other FDA panels and such other persons recruited from the academic and private sectors or other appropriate organizations.

If the dispute resolution mechanism is to be viewed as fair, it is essential that FDA appoint independent experts from outside of FDA to at least half of the panel memberships. Similarly, if the imposition of postmarket surveillance beyond the statutorily allowed three years is to be other than unilateral, it is essential that the dispute resolution mechanism contain at least as many non-agency personnel in the voting positions as FDA personnel.

Other Issues

FDA also states that postmarket surveillance will apply to devices even if they are marketed only for export. Given that FDA's mandate is to protect the public health in the United

States, we question the agency's authority to order postmarket surveillance for export-only devices.

Best regards,

Stephen L. Ferguson

SLF:skr

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